III. Claims 1-7, 11-12, drawn to a compound of formula I, wherein J and K taken together with the two nitrogen atoms form a seven-membered ring, compositions thereof, and methods therewith;

IV. Claims 1-7, 11-12, drawn to a compound of formula I, wherein J and K taken together with the two nitrogen atoms form a hetero ring other than the above three groups, compositions thereof, and methods therewith;

V. Claims 8-10, 13-20, drawn to a method of use of compound of formula (I) in combination with various neurotrophic factors classified in various class depending on the choice of the ring formed by J and K.

The undersigned representative of applicants, in a telephone conversation with the Examiner, elected Group II, claims 1-7, 11-12, for further examination. Applicants affirm such election and reserve the right to pursue the unelected claims in continuing applications claiming priority herefrom.

THE AMENDMENTS

Applicant has amended the claims to overcome the Examiner's rejections.

Applicants have canceled without prejudice claims 3, 8-10, 13-20.

Applicant has amended claim 1 to reflect the above election. Specifically, applicants have amended the definition of radical J and K to recite that taken together they form a 6-membered piperazine ring.

Applicants have amended claim 1 to incorporate the limitation that radicals A and B are independently selected from "-CH_2-CH_2-E" or "-CH_2-CH_2-CH_2-E". Support for this amendment is found at specification page 13, lines 18-20.

Applicant has amended the definition of radical E in claim 1 to recite "phenyl, furyl, thienyl, pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzimidazolyl, benzothiophenyl, quinolinyl, isoquinolinyl, and benzothiazolyl". Support for this amendment is found at specification page 14, lines 3-9.

Applicants have amended the definition of radical R^6 in Y to delete the embodiment wherein radical R^6 cyclizes with radical D.

Applicants have amended the definition of radical D to delete therefrom "hydrogen" and "E". Applicants have replaced for radical "E" therein the limitation of claim 3. Consistent with this amendment, applicants have canceled claim 3.

Applicant has amended claim 1 to delete the proviso with respect to radical J. This proviso was inadvertent and the deletion rectifies the error.

These amendments are further discussed below in the context of the Examiner's objections.

THE REJECTIONS

1. 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-7, 11-12 under 35 U.S.C. § 112, second paragraph, asserting that these claims are indefinite. The specific rejections are enumerated below for the relevant claims.

(a) The Examiner asserts that the phrase "derivatives thereof" in claim 1 renders the claim indefinite.

Applicants have obviated the Examiner's rejection by deleting the phrase "derivatives thereof" and replaced therefore the phrase "salts thereof". Support for this amendment is found in the specification at page 19, lines 4-6.

(b) The Examiner asserts that the proviso in claim 1 relating to radical J is indefinite.

Applicants have amended claim 1 to delete this proviso. The proviso was inadvertently entered in claim 1, and this amendment rectifies this error.

(c) The Examiner asserts that claims 11-12 are indefinite because they do not specify the amounts used in the claimed methods, e.g., therapeutically effective amounts.

Applicants have amended claims 11-12 to recite that the claimed methods use "therapeutically effective amounts" of the compounds of the present invention.

2. 35 U.S.C. § 102

The Examiner has rejected claims 1-7, and 11 under 35 U.S.C. § 102, as being anticipated by the prior art. Each of the documents cited by the Examiner is addressed individually below.

(a) The Examiner has rejected claim 1 as being anticipated by United States patent 4,379,152 (hereinafter "Saikawa"). Applicants traverse in light of the above amendments.

As noted above, applicants have amended the scope of compound of formula (I). Specifically, radical D, as amended, cannot be hydrogen. Consequently, the compounds of Saikawa do not fall within the scope of claim 1, as amended. Claims 2, 4-7, and 11-12 depend either directly or indirectly from claim 1. Consequently, they, too, are patentably distinct from Saikawa.

(b) The Examiner has rejected claim 1 as being anticipated by United States statutory invention registration US H2007 H (hereinafter "Silverman"). Applicants traverse in light of the above amendments.

As noted above, applicants have amended the scope of compound of formula (I), specifically, radicals A, B, and D.

Radicals A and B, as amended, are independently aryl-alkyl groups, specifically, either "-CH_2-CH_2-E" or "-CH_2-CH_2-CH_2-E". In Silverman, column 1, line 20, first formula, the corresponding radical R cannot be bis(aryl-alkyl) substituted methine (-CH-) group.

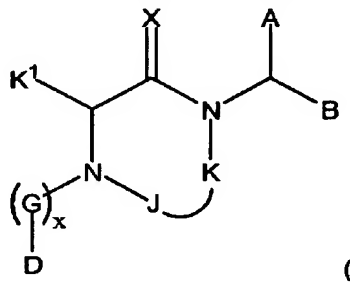
Similarly, because radical D, as amended above, cannot be hydrogen, formula F in Silverman (column 4, line 65) does not fall within claim 1 herein, as amended. Also, formula O of Silverman, too, does not fall within claim 1, as amended. Formula O of Silverman requires the presence of R^3 and R^4 on the methine carbon attached to the ring nitrogen. Each of R^3 and R^4 are defined as optionally substituted phenyl. However, radicals A and B herein, as amended, are defined as aryl-alkyl, specifically, as "-CH_2-CH_2-E" or "-CH_2-CH_2-CH_2-E". Thus, formula O of Silverman does not fall within claim 1, as amended.

For the above reasons, Silverman does not anticipate claim 1, as amended. Claims 2, 4-7, and 11-12 depend either directly or indirectly from claim 1. Consequently, they, too, are patentably distinct from Silverman.

(c) The Examiner has rejected claims 1 and 7 as being anticipated by Hori et al, JP 50 130773, CA 85:33075, 1976 (hereinafter "Hori").

Hori dicloses three compounds, namely, (R,S)-piperazinone-1,4-bis(1,2-diphenylethyl), (R,R)-piperazinone-1,4-bis(1,2-diphenylethyl), and [S-(R,R)]-

piperazinone-1,4-bis(1,2-diphenylethyl). Each of these three compounds contains a 1,2-diphenylethyl [-CH(Ph)-CH_2-Ph] moiety on the ring nitrogen atom adjacent to the carbonyl on the piperazinone ring. In contrast, in formula 1 of the present invention, as amended, that corresponding ring nitrogen atom is attached to a methine (CH) group substituted with radicals A and B, as shown below:



(I).

Each of radicals A and B in claim 1, as amended, is independently -CH_2-CH_2-E or -CH_2-CH_2-CH_2-E. Neither embodiment of radicals A and B will result in a 1,2-diphenyl ethyl [-CH(Ph)-CH_2-Ph] moiety attached to the ring nitrogen. For this reason, the compounds of Hori do not fall within claim 1, as amended.

(d) The Examiner asserts that claims 1 and 7 are anticipated by Choi et al., J. Med. Chem. 42(18), 3647-3657 (hereinafter "Choi"). Applicants traverse in light of the above amendments.

Choi discloses a piperazinone derivative with a phenylpropyl next to the ring carbonyl (compd. 25 therein) or [bis-(4-fluorophenyl)methoxy]-ethyl (compd. 27 therein). As noted above, neither embodiment of radicals A and B, as amended, will result in compd. 25 or compd. 27 of document D2. For this reason, the compounds of Choi do not fall within claim 1, as amended.

(e) The Examiner asserts that claims 1 and 7 are anticipated by Tsizin, Yu, et al., Med. Parazitol. Parazit. Bolezni, 1991, (6), 50-52, Chem. Abs., (hereinafter "Tsizin")[1]. Applicants traverse in light of the above amendments.

Tsizin discloses seven piperazinone derivatives (compounds 4-10 therein). Each of these have attached to the ring nitrogen atom adjacent to the ring carbonyl either a phenylmethyl, phenylethyl, or ethyl. As noted above, neither embodiment of radicals A and B will result in a phenylmethyl, phenylethyl, or ethyl moiety attached

to the ring nitrogen. For this reason, the compounds of Tsizin do not fall within claim 1, as amended.

(f) The Examiner asserts that PCT Publication WO 97/16446 (hereinafter "Chambers") anticipages claim 1. Applicants traverse in light of the above amendments.

Chambers discloses "piperazinones, homopiperazinones and their thione analogues". In each of these compounds, the moiety corresponding to radical D of the present invention is a bicyclic heterocyclic ring system. In contrast, in claim 1, as amended, radical D is either phenyl or pyridyl with optional substituents. Consequently, the compounds of Chambers do not fall within the scope of claim 1, as amended.

(g) The Examiner asserts that claims 1, 7, and 11 are anticipated by European application EP 0 289 227 (hereinafter "Pascal"). Applicants traverse in light of the above amendments.

Formula A of Pascal, page 4, line 15, requires that R4 and R5 therein be an aryl group. The corresponding moieties in compound of formula (I) in claim 1 herein, as amended, namely, radicals A and B, are aryl alkyl. Specifically, radicals A and B, as amended, are independently $-CH_2-CH_2-E$ or $-CH_2-CH_2-CH_2-E$. Consequently, claim 1 as amended is patentably distinct over Pascal. Because claims 7 and 11 indirectly depend upon claim 1, they, too, are distinct over Pascal.

For the above reasons, applicants submit that none of the cited documents anticipate claims 1, 2, 4-7, 11-12, as amended. Consequently, applicants request that the Examiner withdraw the 35 U.S.C. § 102 rejection.

3. Claim Objections

The Examiner has objected to claims 11-12 under 37 C.F.R. 1.75(c) as being in improper form because claim 11 depends from any one of claims 1-6, and claim 3 is multiply dependent.

---

[1] The Office Action recites Hori duplicatively in this rejection. Applicants presume that the Examiner intended to recite Tsizin, which was also cited in applicants' Information Disclosure Statement.

As noted above, applicants have canceled claim 3. Accordingly, applicants have deleted from claim 11 its dependency on claim 3. Applicants request that the Examiner withdraw this objection.

CONCLUSION

Applicant requests that the Examiner enter the above amendments, consider the accompanying arguments and allow the claims to pass to issue. Should the Examiner believe that a telephonic interview would expedite the prosecution of the present application, he is invited to contact the undersigned at any time.

Respectfully submitted,

Nandakumar Govindaswamy
Limited Recognition
Attorney for Applicants
Vertex Pharmaceuticals Inc.
130 Waverly Street
Cambridge, MA 02139-4242
Tel.: (617) 444-6619
Fax: (617) 444-6483